EXHIBIT 5

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AAMI STWG61, AAMI Chemical Sterilants Hospital Practices Working Group

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Comments by L. Muscarella (Custom Ultrasonics) on AAMI TIR7:1999, *Chemical Sterilants and Sterilization Methods: A Guide to Selection and Use*

Note: AAMI TIR 7 was approved in 1999. AAMI policies and procedures require that AAMI Technical Information Reports (TIRs) be reviewed every three years to determine whether they are still current. The responsible committee or working group can decide that no change is necessary to a TIR, that the TIR should be revised, that the TIR should be withdrawn, or that a full consensus standard or recommended practice should be developed to replace the report.

The AAMI Chemical Sterilants Hospital Practices Working Group will consider the status of AAMI TIR 7:1999, *Chemical Sterilants and Sterilization Methods: A Guide to Selection and Use*, at its meeting on Tuesday, 8 October 2002 and will make a decision as to the TIR's future.

After the approval of AAMI TIR 7 in 1999, comments on the document were received from Dr. Lawrence F. Muscarella, PhD. Although late, these comments were considered and a response was sent to Dr. Muscarella. At that time it was decided that no change to the TIR was needed as a result of Mr. Muscarella's comments.

Because of his earlier objection to the TIR, however, AAMI Staff contacted Dr. Muscarella concerning the pending periodic review of AAMI/TIR 7:1999. Dr. Muscarella was invited to restate and resubmit his comments for the consideration of the Working Group. Enclosed are his comments (correspondence of 11 July 2002 and e-mail of 15 July 2002) which will be considered by the Chemical Sterilants Hospital Practices Working Group, during its deliberations on 8 October 2002.

Anyone wishing to submit additional comments on AAMI TIR 1999 or to respond to Dr.Muscarella's comments should send them to my attention at jlewelling@aami.org by 26 September 2002.

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General Comments (comment type "G"):

In the next section, *Specific Comments*, I provide my specific comments to this TIR, which I will refer to interchangeably in my responses below as "TIR," "document," or "draft." In this section, I provide a background discuss and my *General Comments* to this TIR.

First, as I recently expressed to Mr. Michael Miller, the president of AAMI, organizations like AAMI need to rise above corporate marketing and advertising hoopla and consider the implications of its publications on patient safety. The goal of my comments expressed in this letter is to ensure that the TIR's conclusions are supportable and corroborated by independent data. When they are not, I have suggested they be modified or removed. Apparently AMMI has heard my voice and is now willing to respect my opinion, and I thank this organization for giving me the opportunity to review and comment on this TIR.

Second, the position of AAMI needs to be more sensitive to how its TIR and other documents can and will be used in the marketplace. Specifically, AAMI should consider abandoning its clear acceptance as gospel a FDA clearance (refer to attached letter AAMI wrote to me, dated 2000-04-03). Just because the FDA clears a device's labeling for a specific claim does *not* make the claim in and of itself valid. Subsequent data collected after a device appears on the market (e.g., post-clearance data) often reveal weaknesses and in some cases may show that the device's label claims are false and misleading. A 510(k) clearance only states that the device is substantially equivalent to a predict device on the market; it does not, as AAMI's letter to me suggests, confer as fact and credible all of the device's label claims.

Third, the document displays a few striking inconsistencies. For example, in sections 6.2 and 6.4, the document asks very good questions vis-à-vis the selection of sterilizing agents, placing significant emphasis (and rightly so) on the importance of the availability of test data that demonstrate a sterilizing agent's effectiveness. Yet in the document's controversial section 4.3.3, which provides text that reads: "*The cycle (referring to the Steris System 1) includes rinsing with sterile water produced by passing tap water through a 0.2 micron filtration membrane,*" the ball is dropped, as the document fails to apply the same standard of accountability that it applies to sterilizing agents to water filtration systems that claim to produce sterile water. The document's claim that 0.2 micron filters produce sterile water is taken for granted and never challenged. Indeed, nowhere in this document is a reference provided that would permit the reader to evaluate published data (of which there are none) that demonstrate a water filtration system can produce sterile water from a hospital's tap. If a revised draft of this TIR is to include this reference to the production of sterile water using a bacterial water filter, please add the references you have on file to support such a claim. (Good luck!)

I am fully aware that this document does not pretend or claim to discuss in detail water filtration systems and their effectiveness. But because the document in section 4.3.3 has introduced this topic and implicitly endorsed this sterile water claim, it will need to be consistent and apply the same standards of proof to water filtration systems that it applies to sterilizing agents. Using the document's own language (see section 6.4.h), it is

necessary for the document to discuss how the "user (would) know if the (water filtration) process (did or) did not 'work.'" I suggest modifying the text by referring to the Steris System 1's rinse water as "filtered water." This may effectively remove at least one of this document's inconsistencies.

Specific Comments:

1. **Annex F: Bibliography (comment type "E"):** I reviewed the bibliography and it is lacking. Refer to the end of this document for relevant references not included in this document. References #1-6 at the end of this letter, among others, discuss the limitations of water filtration systems that use bacterial filter and their failure to produce sterile water from a hospital's tap, as well as the risks to patient safety posed by such erroneous water filter claims.

   Reference #7, found at the end of this letter, should also be added to this document's bibliography, because it provides the rationale for routinely monitoring any water filtration process that claims to produce a sterile product. Indeed, if the rinse water were not monitored, then by default it cannot be assumed to be "sterile" (although it is not necessarily unsafe). Sterilization claims require monitoring. The draft failed to address this issue. I suggest all references to sterile water be removed from the draft, or, the draft needs to include the requisite discussion of the importance of monitoring processes that claim to produce sterile water.

2. **Can water filtration systems produce 'sterile' water? (comment type "T"):** In the letter you wrote to me (see attached), dated 2000-04-03, I would like to comment to your reply: *"The cycle (referring to the Steris System 1) includes rinsing with sterile water produced by passing tap water through a 0.2 micron filtration membrane. This statement is a verbatim, FDA-cleared label claim and was adopted after extensive discussion by the Working Group. As far as we can determine, the descriptions of this product ... in this document are accurate, both technically and from a regulatory standpoint."*

   This reply is of concern, because this statement, which presumably represents the Working Group's consensus opinion, is erroneous, untenable, scientifically indefensible and paradoxically can create a scenario that places patients at a significant risk of infection (refer to reference #6). Indeed, the statement in your letter regarding the effectiveness of water filtration systems is not "accurate."

   Applying the level of accountability the document requires of sterilizing agents also to water filtration systems, I ask what independent published data did AAMI and its Working Group use to conclude in the document that it is accurate to say that the Steris System 1 (or any filtration process that claims to produce sterile water from a hospital's tap) produces "sterile water ... by passing tap water through a 0.2 micron filtration membrane?" I am now, as I was in 1999, concerned that AAMI and its Working Group would adopt as truth this unsupportable position and suggest there are data (when there are not) to support this "sterile" water claim.

Let me be very and respectfully clear: First, there are no independent data in the medical literature that support the production of sterile water (e.g., defined as containing fewer than 10^{-6} CFU/ml and fewer than 5 endotoxin units/ml) by passing unprocessed water (that is, un-sterilized water, such as water that flows though a hospital's tap) through a bacterial (e.g., 0.1 or 0.2 micron) filtration system.

Second, if, for the sake of argument, we were to conclude (erroneously) that the document's reference to the production of sterile water using a bacterial filter were "accurate," then this document is remiss, because it does not provide the requisite discussion of the importance of routinely sampling/monitoring the filtration process, to ensure the conditions for sterility were achieved. Indeed, the routine sampling/monitoring of processes (e.g., steam sterilizers) is a practice recommended by AAMI when sterility or sterilization is claimed. Shouldn't that which applies to one type of process that is designed to produce a sterile product – that is, a steam autoclave – also apply to all others – that is, a filtration process that claims to produce sterile water? To be clear, a filtration process cannot be considered "effective," nor the conditions for "sterilization" achieved, unless the process is routinely monitored using biological indicators. (Refer to reference 7, found at the end of this letter).

I suggest modifying the text by referring to the Steris System 1's rinse water as "filtered water." Alternatively, I suggest all references to sterile water be removed from the draft. This may effectively remove the document's inconsistencies.

3. **The limitations of LCSs ? (comment type "T"):** I would ask AAMI to reconsider this document's depiction of the effectiveness of liquid chemical sterilants (LCSs) and the processes that use them (e.g., Steris System 1). Specifically, I suggest that in this document AAMI consider referring to LCSs as being '100% sporicidal,' modeled after the AOAC's sporicidal test for LCSs, rather than being capable of achieving instrument 'sterilization' (see the TIR's sections: 4.2, 4.3.1). The application of LCSs to instrument sterilization is dubious for several reasons (see references #8-20, found at the end of this letter). Moreover, a sterilization label claim for LCSs is also at odds with the FDA's proposed re-labeling of LCSs, to be announced soon in an ANPR.

   In short, this AAMI document is remiss in that it improperly equates a multi-step sterilization process with known quality controls, such as one that uses steam or ethylene oxide gas in a facility's central supply department, to the single step of immersing the instrument in a LCS. Indeed, these two types of processes (multi-step versus a single-step) are distinctly different and incongruous, and in my opinion the AAMI document needs to make this explicitly clear, which it currently does not do.

   There are no independent published reports or data anywhere in the medical literature that show LCSs (or any other method/process/agent) can be used to reliably "sterilize" flexible endoscopes or other complex, lumened instruments.

   Therefore, please consider including in the AAMI document a discussion that details the limitations (as well as advantages) of LCSs and how using them to make claims of "sterilization" conveys a false level of sterility assurance that can increase the risk of patient infection (see references #6, 8, 10, and 11, found at the end of this letter).

Also, refer to the FDA's MAUDE for a plethora of reports that document patient infection linked to bronchoscopes, gram-negative bacteria and mycobacteria, and an AER; and the FDA's correspondence to a manufacturer, dated April 23, 2001, which is discussed in reference #6, at the end of this letter.)

I further suggest that AAMI review the current medical literature to understand the limitations of LCSs and liquid-based automated endoscope reprocessors labeled to achieve "sterilization" (see references #8-20, at end of this correspondence); talk to the FDA to understand its current position that opposes the use of LCSs for "sterilizing" flexible endoscopes; and then produce a revised document that is consistent with the FDA – not one, such as the current draft, that is at times at odds with the FDA. Again, differences between the AAMI document and the FDA need to be resolved. This may require that the AAMI document be significantly modified.

4. **AAMI section 3.2 (comment type "T"):** The document does not note that published data supporting log linear kinetics of LCSs are lacking. In fact, this section implies that such data do exist for LCSs that claim to achieve "sterilization." Please change the text accordingly or provide the reference that supports his claim.

5. **AAMI section 3.4 (comment type "T"):** This section is misleading. If a manufacturer submits a 510(k) to the FDA, it does *not* have to "provide evidence of the safety and efficacy of the product." All a manufacturer has to do is show that its device is substantially equivalent to a predicate device – not that it is safe and effective. Please change text accordingly.

6. **AAMI section 4.3.1 and 4.3.3 (comment type "T"):** For many reasons, not the least of which is the "wash-off" effect and the complete violation of the integrity of a biological indicator (BI) when it is removed from its sterile wrapping and placed into the LCS, discussions in this document that refer to the use of BIs for monitoring LCSs are meaningless and should be removed (refer to reference #15). The practice of using a BI to monitor a LCS-based process is flawed and without precedent.

7. **AAMI section 4.3.1 (comment type "T"):** Please remove all references in the document that suggest the use of LCSs for processing dental equipment is acceptable. The CDC and FDA have clearly stated that dental devices, because of their ability to withstand the rigors of pressure and heat, are to be steam sterilized – not processed using a LCS or other low-temperature sterilizing agent.

8. **AAMI section 4.3.2 (comment type "T"):** There seems to be a bias, although subtle at times, expressed throughout this document, to the benefit of one LCS and to the detriment of others. For the integrity of this document, even the appearance of such a bias needs to be removed. What applies to one LCS needs to apply to all others. For example, the end of this section discusses the adverse health effects of glutaraldehyde. But such discussions are not included in the sections that discuss peracetic acid, even though review of the two products' MSDS sheets indicates that peracetic acid is a carcinogen whereas glutaraldehyde is not. Please change text accordingly and treat all LCSs equally.

9. **AAMI section 4.3, 6.5 (comment type "E"):** Please include reference #21, found at the end of this letter, which describes a facility's experience with instrument damage and costly repairs when using peracetic acid. The omission of this reference from this section is striking, particularly in light of reference in section 4.3.4 to hydrogen peroxide being potentially damaging to instrumentation and to the document's clear emphasis on materials compatibility and cost effectiveness (Section 6.5, 6.6, Table 4, and Annex B). It is these types of missteps that suggestion a bias in this document.

10. **AAMI section 5.1 (comment type "T"):** I believe this text is misleading. During the evaluation of a product during the 510(k) process, the FDA does not rely on the submission of safety and efficacy data, as this section suggests. Rather, the manufacturer is only required to provide an application to the FDA that shows its product is substantially equivalent to a predicate device. See section 5.2.2.1, which appears to be accurate.

11. **AAMI section 6.2 (comment types "T" and "E"):** A few important questions to add to the list are the following:

    If the device uses a water filtration system, what are the limitations of the filter(s) (refer to section 6.2.i and apply this same question to the water filtration system)*? How often does the filter(s) need to be changed/replaced? What maintenance procedures are required for the water filtration system and how often must they be performed? If the water filtration system claims to produce 'sterile' water, what controls are in place to ensure that this end product can be reliably and consistently produced* (refer to section 6.2.r)*? Per AAMI's requirements for other sterilization processes* (see section 7.3: "If a water treatment process is used, it should be monitored to ensure that the appropriate water quality is achieved."), *how often is the filtered water to be microbiologically monitored, to ensure the water filtration process is within specification, working properly, and producing sterile water* (refer to sections 6.2.f, 6.3.j, 6.4.e, and, most important, section 6.4.h. Apply these same questions/criteria, which are directed to LCSs, to water filtration systems and their claimed production of 'sterile' water. Rinse water that is not routinely monitored has to be considered unsterile, although not necessarily unsafe)*? What microbiological assay methods are most appropriate to use to "measure or monitor"* (refer to section 6.4.h) *the rinse water to ensure its sterility? To what type of microorganisms should the assay method be sensitive: Mycobacteria? Gram-negative bacteria? Viruses? Endotoxins? What concentrations of these microorganisms are permissible to claim sterility? What concentrations are unacceptable? Is the sterile water produced by this simple filtration process acceptable for hemodialysis applications? And if not, why not?*

    Whereas some of these questions in the draft are appropriately applied to the selection of a sterilizing agent, none are applied to the process that uses a water filtration system to produce 'sterile' water (see section 4.3.3. Please modify the text accordingly to be consistent. The rules that apply in the document to a sterilizing agent should, for consistency and completeness, also apply to a water filtration system. It is surprising that the document does not apply to water filters that which it applies to sterilizing agents.

References

1. Richards J, Spencer R, Fraise A, et al. Rinse water for heat labile endoscopy equipment. *J Hosp Infect* 2002;51:7-16.

2. Cooke RPD, Whymandt-Morris A, Umasankar RS, et al. Bacteria-free water for automatic washer-disinfectors: an impossible dream? *J Hosp Infect* 1998;39:63-5.

3. Humphreys H, Lee JV. Water quality for endoscope washer-disinfectors. *J Hosp Infect* 1999;42:76-8.

4. Phillips G, McEwan H, Butler J. Quality of water in washer-disinfectors. *J Hosp Infect* 1995;31:152-4.

5. Parnell P, Wilcox MH. *Mycobacterium chelonei* and *Acremonium* sp. Isolated from endoscope auto-disinfector rinse water despite daily treatment with chlorine dioxide. *J Hosp Infect* 2001;48:152-4.

6. Muscarella LF. Leading a horse to water: Are crucial lessons in endoscopy and outbreak investigations being learned? *Infect Control Hosp Epidemiol* 2002 July;23(7):XXX-XXX.

7. Muscarella LF. Application of environmental sampling to flexible endoscope reprocessing: the importance of monitoring the rinse water. *Infect Control Hosp Epidemiol* 2002 May;23(5):285-9.

8. Muscarella LF. Labeling of Liquid Chemical Sterilants: Are Modifications Needed? *Infection Control Today.* February 2002.

9. Muscarella LF. High-level disinfection or "sterilization" of endoscopes? *Infect Control Hosp Epidemiol* 1996 Mar;17(3):183-7.

10. Muscarella LF. Are all sterilization processes alike? *AORN J* 1998 May;67(5):966-70, 973-6.

11. Muscarella LF. Anticipated reliability of liquid chemical sterilants. *Am J Infect Control* 1998 Apr;26(2):155-6. Review.

12. Automatic flexible endoscope reprocessors. *Gastrointest Endosc Clin N Am* 2000 Apr;10(2):245-57. Review.

13. Daschner F, Ruden H. Does Steris sterilize? *Infect Control Hosp Epidemiol* 1998 Oct;19(10):740.

14. Daschner F. STERIS SYSTEM 1 in Germany. *Infect Control Hosp Epidemiol* 1994 May;15(5):294, 296.

15. Bond WW. Biological indicators for a liquid chemical sterilizer: a solution to the instrument reprocessing problem? *Infect Control Hosp Epidemiol* 1993 Jun;14(6):309-12.

16. Rutala WA, Gergen MF, Weber DJ. Comparative evaluation of the sporicidal activity of new low-temperature sterilization technologies: ethylene oxide, 2 plasma sterilization systems, and liquid peracetic acid. *Am J Infect Control* 1998 Aug;26(4):393-8.

17. Pappas SA, Schaaff DM, DiCostanzo MB, King FW Jr, Sharp JT. Contamination of flexible fiberoptic bronchoscopes. *Am Rev Respir Dis* 1983 Mar;127(3):391-2.

18. Muscarella LF. Deja Vu...all over again? The importance of instrument drying. *Infect Control Hosp Epidemiol* 2000 Oct;21(10):628-9.

19. Muscarella LF. Limited surveillance in the endoscopic setting: has its time arrived? *Am J Infect Control* 2002 Feb;30(1):66-7.

20. Muscarella LF. Disinfecting endoscopes immediately before the first patient of the day. *AORN J* 2001 Jun;73(6):1159-63.

21. Fuselier H, Liquid sterilization versus high level disinfection in the urologic office. Urology. 1997 Sep;50(3):337-40.